REMARKS/ARGUMENTS

Status of Claims

Allowable Claims

Applicants thank the Office for noting that claim 5 is allowable.

Claims canceled

In the instant amendment, claims: 4, 23, 31, 34, 36, 37, 38, 126, 267, 268, and 269 are canceled, without prejudice or disclaimer. Accordingly, after entry of the instant amendment claims: 1, 2, 3, 5, 6, 10, 13, 21, 22, 27, 40, 41, 42, 45, 47, 106, 128, 151, 167, 197, 259-266, 270, and 271, are pending.

Outstanding objections

Claims 6, 22, 23, and 266 are objected to.

Outstanding rejections

Claims 1-4, 10, 11, 13, 21-23, 27, 31, 34, 36-38, 40-42, 45, 47, 106, 126, 128, 151, 167, 197, 259-265, and 267-271, are rejected under 35 U.S.C. § 112, first paragraph, enablement and written description requirements.

Information Disclosure Statement

Applicants note that an Information Disclosure Statement (IDS) was filed on August 6, 2009, after the mailing of Final Office Action on July 20, 2009, and request consideration of the IDS as filed.

Support for the Claim Amendments

The specification, including the claims as filed, sets forth an extensive description of the invention in the amended claims. Accordingly, Applicants respectfully submit that no new matter is introduced by the instant amendment.

Claim Objections

Claim 6 is objected to for the reasons stated on page 2 of the OA. In brief, the Office alleges that Claim 6 is an improper multiple dependent claim and depends from Claim 4, which is a dependent claim. The instant amendment addresses this issue. For example, Claim 4 is canceled and Claim 6 has been amended such that it depends from Claims 1, 2, 3 or 5, none of which are multiple dependent claims. Therefore, Applicants respectfully request that the objection to Claim 6 be withdrawn.

Claims 22 and 23 are objected to for the reasons stated on pages 2-3 of the OA. In brief, the Office alleges that claim 23 will be a substantial duplicate of Claim 22 if Claim 22 is found allowable. Claim 23 is canceled by the instant amendment; therefore, Applicants respectfully request that the objection to claim 22 be withdrawn.

Claim Rejections Under 35 U.S.C. § 112, first paragraph

Enablement

Claims 1-4, 6, 10, 11, 13, 21-23, 27, 31, 34, 36-38, 40-42, 45, 47, 106, 126, 128, 151, 167, 197, 259-265, and 267-271, are rejected under 35 U.S.C. § 112, first paragraph, enablement requirement for the reasons stated on pages 3-16, of the OA.

The Office acknowledges that the specification is enabling for an isolated polynucleotide of SEQ ID NO:23, encoding a polypeptide of SEQ ID NO:24 having laccase and comprising peroxidase activity, vectors, isolated host cells comprising the polynucleotide and methods for making and using said polypeptide. However, the Office alleges that the specification does not reasonably provide enablement for any isolated polynucleotide having at least 95%-99% sequence identity with an isolated polynucleotide of SEQ ID NO:23 over a region of 1650-1700 residues and encoding a polypeptide having laccase and peroxidase activities, vectors, host cells comprising said polynucleotides and methods for making and using said polypeptides. Further, the Office alleges that undue experimentation would be required to practice the claimed invention.

To address the Office's concerns, the claims have been amended to recite nucleic acids having at least 95% sequence identity to the full length of SEQ ID NO:23, encoding a polypeptide having laccase and comprising peroxidase activity.

The Office alleges that Applicants have not provided enough guidance with regard to which amino acids in the protein's sequence, and the respective codons in its polynucleotide, are tolerant of modification. The Office further alleges that undue experimentation would be required of the skilled artisan to make and use the claimed invention. Applicants respectfully disagree.

It is alleged that the specification fails to provide any guidance with regard to the making of variants and mutants. Further, the Office alleges that the unpredictability of the art precludes predicting function from a polypeptide primary structure. The Office also cites *Guo et al.* to support its prima facie case of lack of enablement alleging, inter alia, that it was not routine to screen for multiple substitutions or multiple modifications of the exemplary sequence to determine the additional species within the scope of the claimed genus. The Office uses Guo to support the allegation that because there is a large number of possible nucleic acid sequence variations, it would require undue experimentation to determine all of the active species within the claimed genus.

In order to make an enablement rejection, the Examiner bears the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. In re Wright, 999 F.2d 1557, 1562 (Fed. Cir. 1993). A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 USC 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained there which must be relied on for enabling support. See also MPEP §2164.04, 8th ed., rev. July 2008.

Applicants respectfully aver that Guo is not sufficient to rebut the instant application's presumption of enablement and therefore cannot support a prima facie case of lack of enablement. Guo developed a mathematical paradigm to quantitate protein tolerance to random sequence changes. Guo's model was developed to understand the probability that a random amino acid replacement will lead to a protein's functional inactivation. While Guo's model does

predict that random codon replacement will generate many inactive variants, in fact, they found 920 active variants. Thus, Guo demonstrates that significant numbers of active variants can be generated using a random mutation and screening protocol. As such, Guo is not sufficient to rebut the presumption of enablement.

The Office acknowledges that methods of producing variants of a known sequence are well known in the art. However, it is alleged that without sufficient guidance, the skilled artisan would be reduced to the necessity of producing and testing virtually infinite possibilities of variants to determine which ones have laccase activity. Applicants respectfully disagree. Procedures for identifying polypeptides having laccase activity were routine in the art at the time of the invention. Further, exemplary assays for identifying polypeptides having laccase activity are described in Examples 1 and 2, starting at paragraph [0626] of the published specification. Further, the specification provides guidance on making variants. Specifically, see e.g. paragraph [0477] which describes consensus sequences among sequences encoding laccases.

Additionally, whether large numbers of compositions must be screened to determine if one can be used to practice the claimed invention is irrelevant to an enablement inquiry. Enablement is not precluded by the necessity to screen large numbers of compositions, as long as that screening is routine. The Fed. Circuit in In re Wands directed that the focus of the enablement inquiry should be whether the experimentation needed to practice the invention is or is not "undue" experimentation. Guidance as to how much experimentation may be needed and still not be "undue" was set forth by the Fed. Circuit in, e.g. Hybritech, Inc. v. Monoclonal Antibodies, Inc. 802 F.2d 1367 (Fed. Cir. 1986).

The proper legal test is that the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., In re Fisher, 427 F.2d 833, 839 (CCPA 1970). Further, the Fed. Circuit in In re Wands stated "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification n question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." 858 F.2d 731, 737 (Fed. Cir. 1988). As the proper legal test is that the scope of enablement must only bear a reasonable correlation to the scope of the claims, methods for making the claimed genus of laccase polynucleotides and polypeptides are sufficiently enabling if a reasonable number of claimed species are successfully

made by protocols known in the art and/or described in the specification. Protocols for screening for laccase activity were well known in the art at the time of the invention, as well as described in the specification. Thus, using the teaching of the specification and other protocols known in the art at the time of the invention, one of ordinary skill in the art could have successfully practiced the invention without undue experimentation, including making and use the claimed genus of laccase encoding polynucleotides without undue experimentation.

Accordingly, the enablement rejection under section 112, first paragraph, can be properly withdrawn.

Written Description

Claims 1-4, 6, 10, 11, 13, 21-23, 27, 31, 34, 36-38, 40-42, 45, 47, 106, 126, 128, 151, 167, 197, 259-265, and 267-271, are rejected under 35 U.S.C. § 112, first paragraph, written description requirement for the reasons stated on pages 16-23, of the OA.

In brief, the Office rejects the claims under 35 U.S.C. § 112, first paragraph, written description requirement for allegedly not conveying to one skilled in the art that the applicant, at the time the application was filed, had possession of the large number of variant polynucleotides encoding polypeptides having laccase and peroxidase activity. Applicants respectfully aver that the claimed invention is sufficiently described in the specification such that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing.

To address the Office's concerns, the claims have been amended to recite nucleic acids with 95% identity to the full length of SEQ ID NO:23, encoding a polypeptide having laccase and comprising peroxidase activity. Applicants respectfully aver that all polynucleotides of the claimed invention are described by structure (the exemplary SEQ ID NO:23, encoding SEQ ID NO:24), a physico-chemical property (polynucleotides having at least 95% sequence identity to SEQ ID NO:23) and function (laccase activity). Applicants respectfully submit that describing a genus of polynucleotides in terms of physico-chemical properties and function satisfies the written description requirement of section 112, first paragraph, as recognized by the USPTO guidelines.

Additionally, Applicants' respectfully aver that it was not necessary for one skilled in the art to know the correlation between structure and function of laccases to be in possession of the invention. One of ordinary skill in the art, using the teaching of the specification, would have been able to make and screen for nucleic acids that encode for variants having at least 95% sequence identity to SEQ ID NO:23.

The Office cites Witkowski et al. to show how even small changes in structure can lead to changes in activity. Witkoski showed that small number of amino acid residue changes in the catalytic site of a family of structurally related enzymes can result in a change in activity. Witkowski noted that beta-ketoacyl synthases involved in the biosynthesis of fatty acids and polyketides exhibit extensive sequence similarity and share a common reaction mechanism. Further, Witkowski also noted that multiple sequence alignments identified catalytic sites and provided the first clues about the possible identities of residues that play critical roles in catalysis. Witkowski's data suggests that most changes in an enzyme's amino acid sequence are not important in determining, or changing its catalytic specificity. Thus, while this reference may show that one single conservative substitution can have a major impact in enzymatic activity, Witkowski's data actually indicates that most changes in an enzyme's amino acid sequence are not important in determining, or changing, its catalytic specificity.

Accordingly, Applicants respectfully submit that the pending claims meet the written description requirement under 35 USC §112, first paragraph, and the rejection may be properly withdrawn

CONCLUSION

In view of the foregoing amendments and remarks, it is believed that after entry of the instant amendment all claims pending in this application will be in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-0661** referencing docket No. D2040-1N; however, the Commissioner is not authorized to charge the issue fee without further authorization.

Respectfully submitted,

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